UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/697,142 | 10/30/2003 | Charles P. Semba | P1989R1 | 9767 |

25213 7590 06/06/2008

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

| EXAMINER | |
|---|---|
| UNDERDAHL, THANE E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1651 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 06/06/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/697,142 | SEMBA, CHARLES P. | |
| | Examiner | Art Unit | |
| | THANE UNDERDAHL | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Applicant's request reply received 3/6/08. Claims 1-9 are pending. No claims are withdrawn. No claims are cancelled. Claims 1 and 7 have been amended. Claims 8 and 9 are new.

**Claim Objections**

Claim 1 is objected to because it contains the typo "0.05 mg mg/mL" [underlined added]. The Examiner will disregard the underlined word in the interest of compact prosecution. However appropriate correction is required.

**New Rejections Necessitated by Amendment**

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amendments to claim 1 render it indefinite. The preamble to the claim is to a solution, but the amendment to the claim includes an indwelling catheter that is obstructed by a blood clot which does not appear to affect the physical properties of the solution. It is unclear to the Examiner the relevance of the catheter to the claimed solution. As discussed in the specification and in the previous Office Action (Mailed 8/24/07) solutions of tenecteplase are known to dissolve fibrin bound blood clots. It appears that the amendment to the claim 1 includes a step where the tenecteplase solution dissolves a fibrin bound blood clot that has been in the catheter for at least about 5 days. However this is confusing since claim 1 is to a composition, specifically a

tenecteplase solution, and not a method for dissolving blood clots in catheters. These limitations render claim 1 indefinite since it is unclear how the catheter provides a structural component to the solution claimed in the preamble of claim 1. Since the dependant claims 1-6 do not clarify this point they too are rendered indefinite by the amendment to claim 1.

In the interest of compact prosecution, the claim 1 will read on a tenecteplase in a solution of sterile water or bacteriostatic water or normal saline at a concentration of 0.01 to 0.05 mg/mL.

Similar confusion arises with claim 7-9. Claim 7 is to a tenecteplase solution composition in a catheter and the new limitations as well as the new claims 8 and 9 are draw to method steps that uses the tenecteplase solution to dissolve blood clots in the catheters. Again since it is unclear how the catheter physically alters the tenecteplase solution it is unclear how these new amendments limit the claimed composition.

In the interest of compact prosecution, claim 7-9 will read will read on a tenecteplase in a solution of sterile water or bacteriostatic water or normal saline at a concentration of 0.01 to 0.05 mg/mL that is capable of dissolving blood clots that are several days old.

## Response to Applicant's Arguments— 35 U.S.C § 103

In the response submitted by the Applicant, the 35 U.S.C § 103 (a) rejection of claims 1-7 over Sandbaek et al. as supported by DrugBank in view of Graney et al. were considered but not found persuasive.

The Applicant argues that the new limitations limiting the tenecteplase solution in a catheter that is obstructed by a fibrogen bound blood clot overcome the teachings of the above references. However as described above these limitations render the claims indefinite since it is unclear how they further limit the solution. The claims are drawn to a solution to tenecteplase in various liquid carriers. The physical properties of a solution of tenecteplase are the same if stored in a vial, test tube, culture flask, bag, syringe or indeed a catheter since the activity of the tenecteplase solution is not effected by the container. Also, the limitation that the solution can dissolve a fibrin bound blood clot is an intended result that can inherently be achieved by the enzyme whose activity indeed dissolves fibrin bound blood clots. Art reading on a tenecteplase solution will also read on these limitations as well since the enzyme activity of tenecteplase will dissolve blood clots.

The Applicant argues that altephase and telectephase are not to be considered as equivalents. The Applicant argues that the lower potency of altephase would not dissolve a fibrin bound blood clot at the concentrations limited in the claims. The Applicant does not provide any support for these statements. Sandbaek et al. clearly is able to dissolve blood clots that are 2-30 days old (paragraph bridging page 87 col 2 and page 88 col 1) using altephase the within several hours (page 88, col 1 Intra-arterial thrombolysis). Clearly from the teachings of Sandbaek et al. altephase has sufficient potency to dissolve blood clots at least 5 days old.

The Applicant argues that altephase cannot be used in a “dynamic therapeutic setting” to remove blood clots in an indwelling catheter. This argument is not

commensurate with the scope of the claims since the claims are to a solution and not a method of removing blood clots in an indwelling catheter.

Therefore the rejection stands and is repeated below and are applied to new claims 8 and 9.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sandbaek et al. (Blood Coagulation and Fibrinolysis, 1999) as supported by DrugBank (def "Tenecteplase") in view of Graney et al. (Australian Patent AU-B-42810, published 1992).

These claims are drawn to a composition containing about 0.01 to 0.05 mg/mL of Tenecteplase in sterile water or bacteriostatic water and normal saline. Claims 2-5 further limit the range of the highest concentration of Tenecteplase in solution to about 0.04 mg/mL, 0.03 mg/mL, 0.02 mg/mL, 0.015 respectively. Claim 6 further limits the Tenecteplase be in sterile water. Claim 7 limits the composition of claim 1 further comprises an indwelling catheter.

Sandbaek et al. teach a concentration of Alteplase in saline at a final concentration of 0.02 mg/mL and is administered by an indwelling catheter (page 88, col 1, "Intra-arterial thrombolysis") to dissolve fibrin bound blood clots that are 2-30 days old

(page 87 col 2 to page 88 col 1). Alteplase is an art recognized equivalent for the same purpose as Tenecteplase (M.P.E.P. § 2144.06) since both have the same activity to dissolve blood clots (see OA mailed 8/24/07 page 2 to 3). Sandbaek et al. does not teach the limitation of claim 5 that the concentration of Tenecteplase is about 0.01 to 0.015. However, the M.P.E.P. § 2145.05 state:

"a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties."

Also while the Sandbaek et al. above teaches the components of the composition of claim 1 they do not teach the concentration limited by claim 5. However, M.P.E.P. § 2144.05 II states:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical.

Absent any teaching of criticality by the applicant concerning the concentration of Tenecteplase listed in claim 5 for the composition of claim 1, it would be *prima facie* obvious that one of ordinary skill in the art would recognize that the amounts listed in claim 5 are result effective variables whose ratio and concentration are a matter of routine optimization.

Also while Sandbaek et al. teach their composition in saline, they do not provide the details on the composition of the saline and thus do not anticipate the limitation of sterile water for injection or bacteriostatic water for injection and normal saline. This is taught by Graney et al.

Graney et al. teach that Tenecteplase (called the synonym tPA or tissue plasminogen activator or Alteplase by Graney, page 7, lines 1-2) can be included in compositions where the solvent carrier is sterile water (page 7, line 8) or distilled water, Ringer's solution as well as saline and other conventional carriers (page 8, lines 19 and 20). Therefore Graney et al. teach that saline as well as sterile water for injection and other conventional pharmaceutical carriers can be used interchangeably to dissolve and administer Tenecteplase and are therefore art recognized equivalents for the same purpose and it would be obvious for one of ordinary skill in the art to substitute saline from sterile water for injection (M.P.E.P. § 2144.06).

Therefore, the invention as a whole would have been prima facie obvious at the time of filing in view of the references listed above and as such claims 1-9 are not allowable.

**In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure**, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Thane Underdahl
Art Unit 1651